

Death Ambivalence and Treatment Seeking: Suicidality in Opiate Addiction

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Abstract

Purpose of review Rates of suicide and opiate overdose have recently skyrocketed in the USA. In light of impulsivity and impaired motivation common in people with substance use disorders, suicidality is common in addiction.

Recent findings Chart review surveys indicate two primary suicidal populations that are important to distinguish for clinical practice and healthcare policy. One group is heavily composed of people with substance use disorders, in whom chronic compulsive use fosters a numb *ambivalence* about death (low death intentionality). Many of these individuals with opiate use disorder (OUD) exaggerate suicidality to get prompt psychiatric care to treat the OUD. The second group is composed of those who have comorbid psychiatric disorders and/or chronic pain who have a higher intent to die consistent with traditionally understood suicide risk factors.

Summary We contend that easier access to outpatient opiate agonist treatment would avoid unnecessary hospitalizations for death-ambivalent OUD patients and for OUD patients in either group. First-line treatment with an opioid agonist has high potential to effectively treat suicidal ideation as a secondary benefit.

Introduction

The USA has recently experienced a 30-year high in suicide rates [1] and rates of unintentional opiate overdose (US Centers for Disease Control). These trends

have been framed as a public health emergency and have stalled an upward trend in life expectancy in white males [2]. This review is devoted to understanding the suicidal

individual with opiate use disorder (OUD) as a unique type of patient who requires a distinct therapeutic approach that centers on treating the addiction, wherein the reduction in suicidality may frequently follow due to improvements in psychosocial circumstances as well as potential direct antidepressant effects of buprenorphine (BUP). From a systems perspective, it is an effort to highlight the need for changes in healthcare policy that will eliminate incentives for OUD patients to exaggerate suicidality to promptly obtain medication-assisted treatment (MAT) for OUD.

Overview of suicidality and substance use disorders

Suicidal ideation is common in patients with OUD. According to data from the Centers for Disease Control (CDC), 12% of opioid overdose deaths in the USA were determined to be completed suicides [3] although these data refer to cause of death and are not specific to individuals with OUD. Among respondents to the National Survey on Drug Use and Health (NSDUH; SAMHSA) with histories of non-medical (e.g., diverted) prescription opiate use, approximately 7% of former-users, 11% of current long-term users, and 9% of recently initiating users reported past-year suicidal ideation, compared to only 3% of never-users. Among these individuals with past-year SI, a greater proportion of persistent (17%) and recent-onset (19%) users reported a suicide attempt, as compared with former-users (7%) and never-users (11%) [4]. Injection opiate users show even higher rates of suicidality [5], suggestive of greater psychiatric comorbidity and indifference to self-harm. Similarly, drug abuse symptomatology is more common in suicide attempt survivors. In an analysis of the most recent 314,881 respondents to the NSDUH, individuals reporting past-year suicide attempts (0.45% of the sample) were at least three times more likely to also endorse multiple symptoms of a substance use disorder (SUD), especially heroin use disorder and “pain reliever” use disorder (approximately seven times more likely than in non-attempters).

Substance abuse is linked to a certain class of suicide attempt. Since the 1960s, there have been several attempts to sub-categorize people who attempt suicide, based on attempt severity or on broad personality features. For example, Paykel and Rassaby [6] reported that attempts clustered into three groups distinguished by low lethality (defined entirely by drug overdose as means of attempt) versus higher levels of chronicity and lethality, with corresponding low versus high death intentionality. This three-group solution was strikingly replicated in a more recent comprehensive study [7] that featured detailed suicidality, trauma, and personality questionnaires in over 1000 consecutively hospitalized people with suicide attempts. Roughly, 60% of these individuals were classified into an “impulsive-ambivalent” group with low-lethality attempts following minimal premeditation. Another ~36% fell into a “well-planned” group, with more premeditation and attempt lethality. Finally, 4% fell into severe group characterized by multiple attempts initiated early in life. The impulsive-ambivalent group had higher rates of (interview-reported) use of alcohol and other drug uses in order to facilitate implementation of the attempt than the well-planned group. Another survey of hospital-admitted suicide attempt survivors showed an inverse relationship between lethality of attempt and impulsivity (lack of

premeditation) [8]. Further complicating matters, limited access to treatment for OUD may contribute to over-reporting of SI to gain access to immediate care on mental health units. Once admitted, symptoms of opioid withdrawal are addressed. In sum, there is a linkage between addiction and a low intentionality and unpremeditated subtype of suicidality that may require targeted treatment and healthcare policy change for the OUD population.

The clinical presentation of the death-ambivalent OUD patient

We posit that this “death ambivalence” is essentially a non-premeditated flavor of suicidality. Indeed, Neale [9] observed that in many cases, intentional drug overdoses were characterized by the *absence* of an unambiguous intent to die. This observation was illustrated in unstructured recollections of opiate overdoses in 36 veterans, including the distal and proximal circumstances that led to them [10••], including “It’s like we just don’t care. We just don’t care because the emptiness is so big that we want to fill it up a bit,” army veteran, as interviewed and cited in [10••]. Whereas only one overdose was an intentional suicide attempt, several participants reported a general ambivalence about death, and Bennett et al. suggested that typologies of suicidality should make a distinction along a spectrum of ambivalence versus active intent. Non-premeditated suicidality may be particularly characteristic of frequent users of SUD treatment services in that low levels of premeditation (assessed with a commonly used impulsivity survey) are particularly characteristic of patients who respond poorly to SUD treatment, where this personality trait does not appreciably change with treatment [11].

Blunted recruitment of motivational neurocircuitry by non-drug rewards in both animal models and in human functional neuroimaging of addiction [12] and depression [13•] provides a mechanism for ambivalence to life. A seminal “reward deficiency hypothesis” of addiction [14] posits that addiction is maintained due to the ablation of motivational neurocircuitry by chronic binge substance use, such that natural rewards no longer yield pleasure. Therefore, only the powerful acute effects of abused substances to release midbrain dopamine are sufficient to elicit motivation—in which addicted individuals use substances to just feel normal for a time. Indeed, an elegant “mega-analysis” that incorporated brain activation maps from cross-sectional comparisons between substance abusers and controls performing reward tasks during fMRI indicated that addiction is characterized by a blunted anticipatory response of mesolimbic incentive neurocircuitry to non-drug rewards [15•]. It stands to reason that reduced motivational impact of non-drug reward prospects such as positive social interactions would lend itself to a “nothing to live for” death ambivalence in OUD. Other underpinnings of the poorly planned suicidality of OUD individuals include impulsivity characteristic of numerous addictions [16] in tandem with a propensity of individuals with SUD to have their decision-making disproportionately swayed by recent events/circumstances instead of a longer history of outcomes [17].

Death ambivalence in addiction, as a special subtype of suicidal ideation, thus requires a different treatment approach, wherein suicide risk might abate as a secondary effect of successful treatment of the addiction (as the primary issue) such as with opiate substitution therapy. First, opiate maintenance therapy may

reduce the psychosocial problems that instigate feelings of hopelessness. Second, the anhedonic dopaminergic neurocircuitry that has been ablated by chronic intoxication may recover with extended time with evidence-based pharmacotherapy for OUD.

Chronic pain and other circumstantial triggers in OUD

Not all suicidality in OUD is characterized by death ambivalence, however. It is well established that current life stressors such as divorce or job loss are environmental risk factors for suicidality. Of note, loss of relationships and employment are often a consequence of OUD. One study of survivors of opioid overdose identified problems with interpersonal relationships as the primary stressor contributing to an intentional OD [18]. Another factor to consider is the social isolation often preferred in opiate abuse (relative to “clubbing” with stimulants) that introduces another critical psychosocial risk factor for suicide [19]. However, the most powerful *enduring* environmental exposure that predisposes to both substance abuse and suicidality is a history of physical, sexual, or emotional trauma [20] (especially in women) [21]. Longitudinal studies have shown that childhood trauma is predictive of increased odds of suicide attempt in adolescence or young adulthood [22, 23]. Finally, some OUD individuals are at increased risk of more intentional suicide by opioid overdose due to previous suicide attempts, depression, and/or other psychiatric diagnoses [24].

Another risk group in OUD is composed of patients originally prescribed opioids for pain during the surge in opiate prescribing in the USA. Although these are more “neurotypical” individuals who followed an iatrogenic progression to heroin addiction, this progression has been shown to be more common in individuals with histories of mood symptomatology [25] and is a departure from the typical progression to illicit drug use from deviant behavior in adolescence [26]. For example, a medical record probe of older Americans in a longitudinal cohort indicated that histories of depression and especially suicide attempts were linked to increased opiate prescription rates, with no differences in medical severity [27]. Madadi et al. noted that of the 214 deaths ruled to be suicides by opioid overdose over a 2-year time frame (06–08), approximately half had chronic pain [24].

Treatment

Medication-assisted therapy (MAT) has been shown to be highly effective in the treatment of OUD [28]. This does not eliminate benefits from non-opioid replacement therapies that have shown initial signs that opiate abstinence is linked to functional recovery of brain reward processes. Bunce et al. [29] reported that cortisol levels, and sleep activity prefrontal cortex activation and acoustic startle responses to natural reward cues among opiate users in residential treatment directly correlated with the number of days since last opiate use. MAT offers the potential for pharmacotherapy as a stand-alone treatment option in addition to recognizing the benefits of behavioral therapies. Access to MAT for OUD has been shown to increase desired treatment outcomes in the areas of physical, social, and psychological health [30] and therefore requires

serious consideration as a critical component in the mitigation of suicide for individuals with opioid use disorders.

Under current Federal regulations, buprenorphine (BUP) is an attractive option for opioid replacement pharmacotherapy, as it can be readily incorporated in various clinical settings to improve treatment access. BUP is a strong μ -opioid receptor partial agonist. It is also a weaker partial agonist (functional antagonist) of the κ -opioid receptor and an antagonist of the δ -opioid receptor. Despite the vast public health outreach/education on opioid overdose, and the increasing numbers of Drug Enforcement Agency (DEA)-waivered prescribers providing BUP for OUD, pharmacotherapy surveys of programs and SAMHSA data indicate that a minority of patients receive MAT for OUD [31]. Rural communities continue to have an insufficient distribution of DEA-waivered prescribers, resulting in reduced access to BUP and evidence-based OUD treatments [32]. Andrilla et al. [33] noted that 60% of rural counties in the USA lack a physician with a DEA waiver to prescribe BUP. Another study found that only 3% of primary care physicians (the predominant specialty of physicians in rural America) had received waivers [34]. Even in urban areas, access to MAT may take days, if not weeks. Additional barriers to accessing agonist and antagonist medication include, though not limited to, belief that abstinence is the best option, families requesting “drug-free” treatment, staff resistance to medication for SUD recovery, cost of the medications, and lack of prescribers [35].

Access to methadone for treatment of OUD has challenges as well, with the Veterans Health Administration (VHA) operating only 32 opioid treatment programs (OTPs) prescribing methadone for OUD, less than one per state. Although a few additional VHA facilitates work with local community clinics to provide services, there are still large gaps in access to OTPs for veterans [36]. In 2017, the VHA was treating 35% of patients diagnosed with OUD with medication, 34% with either buprenorphine or methadone, and 1% with injectable naltrexone [31].

We contend that these barriers to evidence-based pharmacotherapies often lead to an over reporting of SI in the SUD population, because some individuals with OUD are desperate for access to treatment and are aware that reporting an intent to die through suicide will lead to a psychiatric admission. Once admitted, the symptoms of opioid withdrawal will be addressed. In some instances, an accelerated referral to OUD treatment may occur as part of a disposition plan. Because this represents a substantial waste of clinical resources in those cases where actual intent to die is minimal, systematic research on potential over-reporting or exaggeration of suicidal ideation in this population is warranted.

Benefits of MAT beyond OUD treatment

Several recent studies have reported benefits of BUP for psychiatric symptoms and/or pain management that co-occur with OUD. These reports have implications for mitigation of suicide risk in patients with OUD. Although these studies were designed with a mix of participants (including those with and without a SUD), they provide further evidence of the potential benefits of

treating OUD with pharmacotherapy as a first-line treatment targeting desired outcomes for OUD and comorbid conditions. One such study involved a 4-week trial utilizing ultra-low-dose BUP to treat severely suicidal patients without a diagnosed SUD who had a baseline score of ≥ 11 on the self-report version of the Beck Scale for Suicide Ideation. Initial doses of BUP ranged from 0.1 to 0.2 mg daily (raised by 0.1 or 0.2 mg if an increase was determined necessary), with a maximum dose of 0.8 mg daily. Study findings included greater reduction in the Beck Suicide Ideation Scale scores, along with greater reduction in scores for the Suicide Probability Scale. Although less significant than the reduction in suicidal ideation, a reduction in depressive symptoms was also observed [37•].

Collateral non-OUD benefits of BUP were illustrated in a case study of a patient with OUD-severe, who reported experiencing chronic SI on a daily basis, along with other multiple risk factors including a previous suicide attempt, multiple medical conditions, termination of prescribed opioids for her chronic pain, depression, and bereavement concerns. After 1 week of treatment with BUP/naloxone and a final dose of 16/4 mg daily, her suicidal ideation was abated, pain had reduced, and motivation for pleasurable activities returned. Such improvements could be attributed in part to the direct antidepressant effects of BUP [38] which have been attributed to the δ -opioid receptor antagonist of BUP. Reduced suicidality could also result from follow-on benefits to relationships and maintaining employment due to the cessation of problematic drug use. The authors provided a hypothesis that suicidal ideation, substance use, and pain involve overlapping neural pathways that were jointly benefited by the BUP/naloxone.

Another study of the antidepressant effects of BUP [39] added in a potent μ -opioid antagonist, samidorphan (sam), to counteract the addictive properties while maintaining the antidepressant effects of the BUP. Consistent with other studies looking at the antidepressant effect of BUP, symptoms of depression were reduced by administration of BUP/sam at 1:1 and 8:1 ratios, with the greatest reduction found in those who were in the 1:1 treatment group (BUP/sam 4 mg/4 mg qd 3 days 8 mg/8 mg qd 4 day). The 8:1 BUP/sam group experienced a reduction in symptoms also, though these participants also reported noticeable effects from the buprenorphine [39]. Finally, retrospective study of VHA patients with service in Iraq or Afghanistan who met diagnostic criteria for PTSD, chronic pain, OUD, and other substance use disorders (SUDs) found that veterans who were prescribed BUP showed a 24% improvement in PTSD symptoms compared to an 12% improvement in the control group with PTSD, chronic pain, and SUD who received prescribed opioids of ≥ 50 morphine equivalents daily. The symptom reductions noted were sustained over a 24-month period of time [40].

Patients dependent on heroin who received various addiction therapies within the British National Health System showed a 90% reduction in incidence of suicidal ideation at 9 months of treatment, which was sustained at 18 months [41]. Another longitudinal study of heroin abusers indicated that methadone maintenance treatment (MMT) resulted in a reduction of all-cause mortality [42]. These studies demonstrate the potential for multiple, life-saving, benefits when treating OUD and the common comorbid diagnoses that may increase the risk of suicide by intentional opioid overdose.

These collateral symptomatology improvements have prompted explorations of mechanism. In a study of healthy individuals with limited

psychopathology and no history of SUD, a challenge dose of BUP resulted in a reduction in sensitivity for recognizing fearful facial expressions [43]. The authors posit that acute upregulation of the opioid system reduces fear recognition sensitivity, and believe the long-term administration of BUP may have positive effects in disorders of fear and anxiety [43]. Finally, acute withdrawal from chronic opioids increases the frequency in which users choose to receive small but immediate rewards (both money and opiates) over larger but deferred rewards [44]. BUP maintenance could thus blunt suicidality by preventing a withdrawal-induced cognitive bias that over-emphasizes the (miserable) present over the potential long-term future. It seems likely that future studies of BUP effects, such as in neurotypical individuals and/or conjunction with neuroimaging, will reveal additional mechanisms of collateral psychiatric benefit.

Conclusion

In sum, chart reviews and neurobehavioral research suggest that suicidality in many individuals with SUD may be neurobiologically distinct from the intentional, highly lethal, and premeditated suicidality often found in patients without SUD, due to neurotoxic effects of chronic opiates on non-drug motivation and executive function. These factors yield a propensity for chronic low-grade anhedonia and poorly planned suicide attempts. The experience of many clinicians has fostered a suspicion that in OUD, suicidality is frequently exaggerated or even feigned in contexts in which the individual cannot get prompt addiction care. In other cases, the suicidality is authentic, but characterized by an *ambivalence* about life or death (as opposed to a strong desire to die) in response to chronic addiction-related psychosocial consequences. Current hardships are compounded by tendencies among illicit drug abusers to magnify the impact of very recent events, to find less motivational appeal in non-drug rewards, and for unreflective action.

By extension, care systems devoted to the treatment of suicidality in patients impacted by OUD who present with severe comorbid psychiatric and/or chronic pain should consider how the mood symptomatology may be opiate-induced and should ensure adequate treatment of the addiction with opioid replacement therapies. This approach is opposed to only utilizing traditional psychopharmacological treatment of depression coupled with cognitive therapies that target self-harm. Various studies mentioned within this article have demonstrated benefits of pharmacotherapy with opioid replacement for OUD and the literature on additional benefits for comorbid psychiatric and/or chronic pain is growing. Limited access to pharmacotherapy continues to be a barrier to this evidence-based treatment, along with a familiar cultural bias of treating SUD without medications found in providers, families, and even the patients themselves. Improved access to MAT pharmacotherapy entails additional costs, but would also confer the substantial economic benefit of deterring unnecessary hospitalizations.

This article focused on individuals with OUD in relation to suicide by intentional opioid overdose and did not discuss the disposition of patients without an OUD who have had their opioid treatment changed in response to the opioid overdose epidemic. It is well established that chronic

pain and depression are often comorbid, with approximately 50% of patients in primary care with chronic pain also having some type of depressive disorder, and this percentage increases in those seen in specialty pain clinics [45]. Further research on suicidality in individuals with newly unmanaged chronic pain and research on suicide by opioid overdose in patients without opioid use disorders are warranted.

Compliance with ethical standards

Conflict of interest

Stacey C. Conroy declares that she has no conflict of interest.

James M. Bjork declares that he has no conflict of interest.

Human and animal rights and informed consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

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